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(54) METALLOCENE CATALYST AND PRODUCTION OF POLYOLEFIN

(57)Abstract:

PROBLEM TO BE SOLVED: To polymerize an olefin without using an arom. hydrocarbon and without being accompanied by fouling, by combining a metallocene compd. solubilized by the contact with an organometallic compd. in an aliph. hydrocarbon with a cocatalyst carried by a fine particulate carrier.

SOLUTION: The aliph. hydrocarbon may be alicyclic. Examples of the organometallic compd. are organoaluminum (except aluminoxanes), organolithium, organozinc, and organomagnesium compds. An example of the metallocene compd. is bis(η^5 -cyclopentadienyl)zirconium dichloride. The amt. of the organometallic compd. mixed with the metallocene compd. is 10-800 times that of the transition metal atom of the metallocene compd. The cocatalyst, e.g. methylaluminoxane, is carried by a fine particulate carrier such as silica or alumina.

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handling of relative bulk density, and a polymer adheres to the container wall of a reactor further occurs etc.

[0007] As an attempt which solves this, many approaches of supporting co-catalysts, such as a metallocene compound and aluminoxane, on particle support are proposed. Although these are indicated by JP,61-108610,A, a 61-296008 official report, said 63 -280703 official report, a 63-22804 official report, a 63-51405 official report, a 63-51407 official report, a 63-55403 official report, a 63-61010 official report, a 63-248803 official report, JP,4-100808,A, a 3-74412 official report, a 3-709 official report, said 4 -7306 official report, JP,5-239138,A, JP,5-247128,A, JP,7-10917,A, etc., It is difficult not to fully solve the problem of fouling but to apply these techniques to industrial production.

[0008] The catalyst to which the sum total of the carbon number of the alkyl group permuted by one cyclopentadienyl frame becomes JP,5-339315,A from the metallocene compound which is three or more, and which has a cyclopentadienyl group, and aluminoxane is used, and solution polymerization or the polymerization method which carries out a suspension polymerization is indicated in the olefin under existence of aliphatic hydrocarbon. Although it is possible to carry out the polymerization of the olefin, without using aromatic hydrocarbon by this approach, it is the need of using a special metallocene compound with much substituent. Since such a

metallocene compound has much substituent, easily [manufacture] generally its polymerization activity is low.

[0009] The metallocene solution similar to this invention is indicated by JP,7-2918,A, and the method of making aliphatic hydrocarbon solubilize a poorly soluble metallocene compound is suggested to it. The dialkyl complex of a metallocene is used in this official report, and although such a dialkyl complex of a metallocene is obtained by the reaction of the metallocene compound (a) and alkyl lithium which also use this invention, it needs to pass through two or more processes from a metallocene compound (a), and will become very expensive.

[0010] Still such a dialkyl complex of a metallocene is unstable to especially air and moisture, and is not industrially easy to isolate this and to deal with it. Moreover, the thought of using the indispensable aliphatic hydrocarbon solution of a metallocene compound for this official report in this invention is not indicated at all. That is, even if it uses the aromatic hydrocarbon solution of the metallocene compound in this official report with the co-catalyst supported on particle support, such as JP,61-108610,A, and manufactures polyolefine, it is difficult to control a fouling phenomenon.

[0011] Moreover, the metallocene solution similar to this invention is indicated by JP,8-245714,A, and saving the catalyst which consists of a metallocene compound and aluminoxane by the medium containing the aliphatic hydrocarbon of 70 capacity % is indicated. However, the thought of using aromatic hydrocarbon, such as toluene, also here and using the indispensable aliphatic hydrocarbon solution of a metallocene compound in this invention is not indicated at all. Since the aluminoxane which is a co-catalyst component contains in the solution given [this] in an official report especially, even if it manufactures polyolefine by this solution and the co-catalyst supported on particle support, it is also difficult to obtain not only control of fouling but also a polymer by the shape of a particle.

[0012]

[Problem(s) to be Solved by the Invention] Therefore, without using aromatic hydrocarbon, a polymerization is possible for the technical problem of this invention, and it is to offer the manufacture approach of the polyolefine which does not use aromatic hydrocarbon at the time of the polymerization using the metallocene catalyst with which fouling was controlled, and its catalyst.

[0013]

[Means for Solving the Problem] As a result of inquiring wholeheartedly in view of the above-

mentioned situation, when this invention persons contact the specific metallocene compound which is poorly soluble to aromatic hydrocarbon with an organometallic compound into aliphatic hydrocarbon. The ** which does not use aromatic hydrocarbon by combining the co-catalyst with which the metallocene compound was easily solubilized by aliphatic hydrocarbon in one step, and was further supported this metallocene compound solution and in the shape of particle support, It came to complete a header and this invention for the ability of the polymerization of the olefin to be carried out, without following fouling on a still more unexpected thing.

[0014] namely, this invention -- 1 the (Component A):following general formula (I) -- or (II) --
 $(Cp)(Cp^*)MX_1X_2$ (I)
 $(Cp)(Z)MX_1X_2$ (II)

even when inside of formula, Cp, and Cp* is mutually the same -- you may differ -- the sum total of an each carbon number -- two or less alkyl group -- You may permute by the halogen atom, the aryl group, or the aryl halide radical. They are a cyclopentadienyl group or an indenyl group. Cp and Cp* A carbon atom, The bridge may be constructed by 1-3 atomic groups chosen from a silicon atom, a germanium atom, and a tin atom, and Z is R₁R₂N-, R₁O-, or R₁R₂P. - (R₁ and R₂) it may be mutually the same, or you may differ, and they are the alkyl group of the each carbon numbers 1-2 or an alkylene group, the aryl group of carbon numbers 6-10, an arylene radical, or a silicon content radical. It expressed, R₁ and R₂ may combine with Cp, and M is titanium, a zirconium, or a hafnium. X₁ and X₂ it may be mutually the same, or you may differ, an each hydrogen atom, a halogen atom, an alkoxy group, or an amide group is expressed, and at least one of X₁ and X₂ is a halogen atom. The metallocene compound (a) of aliphatic hydrocarbon poor solubility shown, aliphatic hydrocarbon (b), and an organometallic compound (aluminoxane is removed.) the metallocene compound solution which mixes (c), solubilizes a component (a) for a component (b), and is obtained, and the particle support (e) which supported the component B:co-catalyst component (d) -- since -- the becoming metallocene catalyst.

[0015] 2) A metallocene catalyst given in said 1 by which the bridge is constructed over Cp, Cp*, and Cp and Z by 1-3 atomic groups chosen from a carbon atom, a silicon atom, a germanium atom, and a tin atom.

- 3) A metallocene catalyst given in said 1 or 2 X₁ and whose X₂ are chlorine atoms.
- 4) A metallocene catalyst given in either [whose an organometallic compound (c) is alkylaluminium / said] 1 thru/or 3.
- 5) Offer the manufacture approach of the polyolefine characterized by carrying out bulk polymerization of the olefin to either [said] 1 thru/or 4, without using aromatic hydrocarbon for the bottom of existence of the metallocene catalyst of a publication.

[0016] Hereafter, this invention is explained to a detail. The metallocene compound of (a) aliphatic hydrocarbon poor solubility used for the component (A) of this invention is expressed with the following general formula (I) or (II).

$(Cp)(Cp^*)MX_1X_2$ (I)
 $(Cp)(Z)MX_1X_2$ (II)

[0017] Among a formula, the sum total of the carbon number of two or less cyclopentadienyl group or an alkylation radical may be two or less indenyl group, and may be [Cp and Cp*] mutually the same, or Cp and Cp* may differ. [of the sum total of the carbon number of an alkylation radical] Moreover, Cp and Cp* may have substituents other than an alkylation radical, for example, an aryl group, the aryl halide radical, the halogen, etc. additionally. Specifically, a methylcyclopentadienyl radical, a dimethylcyclopentadienyl radical, an ethylcyclopentadienyl radical, 2-methyl indenyl group, 4-methyl indenyl group, 2, 4-dimethyl indenyl group, a 2-methyl-4-phenyl indenyl group, etc. are mentioned.

[0018] Moreover, the bridge may be constructed over Cp and C₁₋₃ with 1-3 atoms with which each is chosen from a carbon atom, a silicon atom, a germanium atom, and a tin atom. The atomic group which forms such bridge formation is expressed with the following formulas.

[0019] Among a -[Y₁ (R₃R₄)] l[Y₂ (R₅R₆)] m[Y₃ (R₇R₈)] n-type, Y₁, Y₂, and Y₃ express a carbon atom, a silicon atom, a germanium atom, or a tin atom, may be respectively the same or may differ. Y₁, Y₂, and Y₃ are a carbon atom or a silicon atom preferably.

[0020] R₃, R₄, R₅, R₆, R₇, and R₈ are the hydrocarbon group of carbon numbers 1-3, t-butyl, an aryl group, or a halogen, may be respectively the same or may differ. R₃, R₄, R₅, R₆, R₇, and R₈ are the hydrocarbon groups or aryl groups of carbon numbers 1-3 preferably. n is the integer of 1, m, 0, or 1-3, and is 1 <=l+m+n<=3. It is 1 <=l+m+n<=2 preferably.

[0021] As an example of the group which forms these bridge formation, a methylene group, ethylene, an isopropylidene radical, a diphenylmethylen radical, a dimethyl silylene radical, a diphenyl silylene radical, a dimethylgermirene radical, a dimethyl SUTANIREN radical, etc. are raised. Z is R₁R₂N-, R₁O-, and R₁R₂P-. R₁ and R₂ in Z are silicon content radicals, such as the alkyl group of carbon numbers 1-2 or an alkylene group, the aryl group of carbon numbers 6-20, an arylene radical or a trimethylsilyl radical, a dimethyl silylene radical, a phenyl dimethylsilyl radical, and a diphenyl silylene radical, may be mutually the same or may differ all. Moreover, R₁ and R₂ may combine with Cp respectively.

[0022] M is either titanium, a zirconium or a hafnium, is a zirconium or a hafnium preferably, and is a zirconium especially preferably. X₁ and X₂ are chosen from a halogen, a hydrogen atom, an alkoxy group, and an amide group, and at least one is a halogen or a hydrogen atom inside. X₁ and X₂ may be respectively the same, or they may differ. X₁ and X₂ are halogens preferably [both], and they chlorine especially preferably [both].

[0023] As a concrete example of (a) metallocene compound of this invention Screw (eta₅-cyclopentadienyl) zirconium dichloride, screw (eta₅-methylcyclopentadienyl) zirconium dichloride, Screw (eta₅-1, 3-dimethylcyclopentadienyl) zirconium dichloride, Ethylene -1, 2-screw (eta₅-1-indenyl) zirconium dichloride, Dimethyl silylene screw (eta₅-1-indenyl) zirconium dichloride, Ethylene -1, 2-screw [2-methyl-eta₅- (1-indenyl)] zirconium dichloride, Dimethyl silylene screw [2-methyl - (eta₅-1-indenyl)] zirconium dichloride, Ethylene screw [2-methyl-4-phenyl - (eta₅-1-indenyl)] zirconium dichloride, Dimethyl silylene screw [2-methyl-4-phenyl - (eta₅-1-indenyl)] zirconium dichloride, Ethylene screw [2-methyl-4-(1-naphthyl)-(eta₅-1-indenyl)] zirconium dichloride, Dimethyl silylene screw [2-methyl-4-(1-naphthyl)-eta₅-1-indenyl)] zirconium dichloride, isopropylidene cyclopentadienyl (eta₅-9-fluorenyl) zirconium dichloride, such mixture, etc. are raised.)

[0024] In addition, it can be used that neither what transposed the chlorine atom of the above-mentioned example compound to other halogen atoms, nor the thing which transposed the zirconium to titanium or a hafnium has a limit in any way as a metallocene compound (a).

[0025] The aliphatic hydrocarbon (b) used in this invention includes the so-called alicyclic hydrocarbon. As an example of aliphatic hydrocarbon (b), a propane, n-butane, i-butane, N pentane, 2,2-dimethyl propane, 2-methyl pentane, 2, and 2-dimethyl butane, 2, 3-dimethyl butane, 2 and 2, 3-trimethyl butane, 2-methyl pentane, 3-methyl pentane, 2, and 2-dimethyl pentane, 2, 3-dimethyl pentane, 2, 4-dimethyl pentane, cyclopentene, n-hexane, 2-methyl hexane, 3-methyl hexane, a cyclohexane, n-heptane, an octane, Deccan, a dodecane, kerosine, paraffin series oil, such mixture, etc. are mentioned. Since removal from a polymer particle is easy especially, a with a carbon numbers [, such as n-butane, i-butane, a pentane, n-hexane, and a cyclohexane,] of six or less thing is desirable, and especially n-hexane is desirable.

[0026] If polyolefine is manufactured with the metallocene catalyst which used aromatic hydrocarbon instead of aliphatic hydrocarbon, aromatic hydrocarbon not only remains in the polyolefine obtained, but it will become difficult [control of fouling].

[0027] The organometallic compounds (c) used by this invention are organic aluminum except aluminoxane, an organic lithium, organic zinc, an organic magnesium compound, etc. As organic aluminum, for example Trimethylaluminum, triethylaluminum, Tree i-butyl aluminum, tree n-butyl aluminum, tree n-hexyl aluminum, Trialkylaluminums, such as tree n-octyl aluminum; A diethylaluminium chloride, Dialkyl aluminum halide, such as dibutyl aluminum chloride and diethyl aluminum bromide; Ethylaluminium sesquichloride, Aluminum sesquihalide, such as dibutyl aluminum sesquichloride; Ethyl aluminum dichloride, The alkylaluminum halogenated partially, such as butyl aluminum dichloride and ethyl aluminum bromide; A diethyl aluminum hydride, A dibutyl aluminum hydride, an ethyl aluminum dihydrido, a propyl aluminum dihydrido, The alkylaluminum hydrogenated partially, such as a butyl aluminum dihydrido; the alkylaluminum by which alkoxy ** was carried out partially [diethyl aluminum ethoxide, dibutyl aluminum ethoxide, etc.] is mentioned.

[0028] As an organolithium compound, methyl lithium, n-butyl lithium, s-butyl lithium, t-butyl lithium, a phenyl lithium, a benzyl lithium, etc. are mentioned. Dimethyl zinc, diethylzinc, etc. are mentioned as an organic zinc compound. As an organic magnesium compound, n-butyl magnesium chloride, s-butyl magnesium chloride, t-butyl magnesium chloride, A methyl magnesium star's picture, an ethyl magnesium star's picture, n-propyl magnesium star's picture, propyl magnesium star's picture, a vinyl magnesium star's picture, methyl magnesium iodide, butyl ethyl magnesium, etc. are mentioned.

[0029] An organoaluminium compound and an organolithium compound are [among these] desirable, and an organoaluminium compound is still more desirable. Since especially the solubility to aliphatic hydrocarbon is good also in an organolithium compound, the alkyl lithium which has a with a carbon numbers [of n-butyl lithium, s-butyl lithium, t-butyl lithium, etc.] of four or more hydrocarbon group is desirable. In an organoaluminium compound, the organoaluminium compound which has a with a carbon numbers of four or more hydrocarbon group is desirable, and the trialkylaluminium which has a with a carbon numbers [, such as tree i-butyl aluminum, tree n-butyl aluminum, tree n-hexyl aluminum and tree n-octyl aluminum,] of four or more hydrocarbon group is the most desirable.

[0030] It is possible for there to be especially no limit in the method of preparation of the metallocene compound solution of the component (A) in this invention, and to mix said component (a), (b), and (c) by the approach of arbitration. If in charge of mixing, it is usually carried out under inert gas ambient atmospheres, such as nitrogen and an argon.

[0031] It will be (i) if it explains more concretely. How to add aliphatic hydrocarbon (b) and an organometallic compound (c) to a metallocene compound (a) at coincidence, (ii) How to add the aliphatic hydrocarbon (b) solution of an organometallic compound (c) to a metallocene compound (a), How to add aliphatic hydrocarbon (b) and an organometallic compound (c) to a metallocene compound (a) serial, (iii) (iv) How to add an organometallic compound (c) and a metallocene compound (a) to aliphatic hydrocarbon (b) at coincidence, (v) The approach and (vi) which add a metallocene compound (a) in the aliphatic hydrocarbon (b) solution of an organometallic compound (c) It is the approach of adding a metallocene compound (a) and an organometallic compound (c) to aliphatic hydrocarbon (b) serial etc. Moreover, it is also possible to manufacture under existence of the below-mentioned component (B).

[0032] Especially a limit does not have such mixed temperature, the range of it is usually -78 degrees C - 200 degrees C, and the range of it is -30 degrees C - 120 degrees C preferably. Moreover, there is especially no limit, and mixing time is also performed until aliphatic hydrocarbon is mixed with an organometallic compound and a poorly soluble metallocene compound fully dissolves in it.

[0033] In the metallocene compound solution (component (A)) in this invention, it is usually 1 to 10,000 times the mixing ratio of the organometallic compound (c) to a metallocene

compound (a) of this to the transition-metals atom 1 in a metallocene compound, and is it still more preferably five to 2,000 times preferably. [of this] [10 to 800 times]

[0034] Moreover, the concentration of the metallocene compound in a metallocene compound solution (component (A)) is usually the range of 10-6-0.09 mols/l., and is the range of 10-5-0.01 mols/l. preferably. Although even ten to 6 mol/l less than l. is usable, since a lot of solvents are added at the time of a polymerization, a polymerization method may be restricted, or the fall of activity and the fall of molecular weight may take place. Moreover, if l. is exceeded in 0.09 mols /, it will become difficult to obtain a uniform solution.

[0035] Next, the (B) component of this invention is explained. When the component (B) used by this invention contacts metallocene compounds, such as aluminoxane and an organic boron compound, the co-catalyst component (d) which forms a metallocene catalyst is supported on particle support (e), such as a silica. A thing well-known as a co-catalyst component and particle support can use it that there is no limit in any way.

[0036] Aluminoxane is raised as an example of a co-catalyst component (d). As aluminoxane, it is obtained by the reaction of one kind or two kinds or more of trialkylaluminums, and water, and a well-known thing is usable. Specifically, the methyl aluminoxane obtained from one kind of trialkylaluminium, ethyl aluminoxane, butyl aluminoxane, isobutyl aluminoxane, the ethylethyl aluminoxane obtained from two kinds of trialkylaluminums, methylbutyl aluminoxane, methyl isobutyl aluminoxane, etc. are mentioned. Moreover, it is also possible to use what denaturalized by what mixed these plurality, trimethylaluminum, triethylaluminum, triisobutylaluminum, diethyl aluminum chloride, etc. Also in these, methyl aluminoxane, isobutyl aluminoxane, and methyl isobutyl aluminoxane are desirable, and methyl aluminoxane and especially methyl isobutyl aluminoxane are desirable.

[0037] There is an organic boron compound as other examples of a co-catalyst component (d). If shown more concretely, dimethyl anilinium tetrakis pentafluoro borate, Triphenylcarbenium tetrakis pentafluoro borate, triethyl oxonium tetrakis PENTAFURUOROBORATO, The boron or the aluminium compound containing non-coordination nature ion, such as tropylidium tetrakis pentafluoro borate, Nonionic organic boron compounds, such as tris pentafluorophenyl borane, tris (3, 4, 5-trifluoro phenyl) borane, tris (2, 3, 5, 6-tetrafluoro phenyl) borane, and tris (pentafluoro phenoxy) borane, etc. are mentioned.

[0038] These co-catalyst components (d) are used in the form supported on particle support (e). Control of fouling is difficult when not supporting to particle support. As these particle support, the thing of arbitration is usable. Specifically, organic high molecular compounds, such as silicate, such as magnesium silicates, calcium silicate specific silicates, etc., such as metal alkoxides, such as metal hydroxides, such as metal halogenides, such as metallic oxides, such as a silica, an alumina, a titania, a magnesia, and a zirconia, and a magnesium chloride, an aluminum hydroxide, and a magnesium hydroxide, magnesium ethoxide, and magnesium methoxide, a carbonate, a sulfate, a nitrate, acetate, a mica, and talc, polyethylene, polypropylene, and polystyrene, etc. can use it suitably. Silicate, such as magnesium silicates and calcium silicates, such as a silica, an alumina, a mica, and talc, and a specific silicate, is [among these] desirable.

[0039] Although there is especially no limit, the range of the mean particle diameter of these particle support (e) is usually 0.1-2,000 micrometers, and the range of it is 5-100 micrometers still more preferably 1-1,000 micrometers preferably. Moreover, although especially a limit does not have specific surface area, either, it is usually the range of 0.1-2,000m²/g, and it is 10-1,500m²/g preferably, and is the range of 100-1,000m²/g still more preferably.

[0040] As a component (B) which is the particle support (e) which supported said co-catalyst component (d) The thing, tris (pentafluorophenyl) borane which supported methyl aluminoxane on the silica or the alumina, Dimethyl anilinium tetrakis pentafluoro borate, triphenylcarbenium

tetrakis pentafluoro borate, Well-known things, such as triethyl oxonium tetrakis PENTAFURUOROBORATO₄⁻ and N-dimethyl anilinium tris (pentafluorophenyl) [p-(chlorodimethylsilyl) tetrafluoro phenyl] borate, What supported the combinable compound on the silica or the alumina chemically to support, such as N and N-dimethyl anilinium tris (pentafluorophenyl) (p-trichlorosilyl tetrafluoro phenyl) borate, is illustrated.

[0041] What supported methyl aluminoxane and tris (pentafluorophenyl) borane on the silica or the alumina since it was easy is desirable. the inside of these components (B) -- acquisition -- moreover, from there being little especially fouling and the description of the polymer particle obtained being good N and N-dimethyl anilinium tris (pentafluorophenyl) [p-(chlorodimethylsilyl) tetrafluoro phenyl] borate, What supported N and N-dimethyl anilinium tris (pentafluorophenyl) (p-trichlorosilyl tetrafluoro phenyl) borate etc. on the silica or the alumina is desirable.

[0042] Although attained by contacting these by the approach of arbitration, support of a up to [the particle-like support (e) of said co-catalyst component (d)] fully needs to remove this from the (B) component obtained by solid liquid separation, reduced pressure distilling off, etc., when solvents other than aliphatic hydrocarbon are used.

[0043] Although these contact can be performed at the temperature of arbitration in consideration of the conditions of the organic solvent to be used or others, it is usually carried out in -80 degrees C - 300 degrees C. The range where contact temperature is desirable is -50 degrees C - 200 degrees C, and the still more desirable range is 0 degree C - 150 degrees C. Moreover, although it is possible for there to be especially no limit in the amount used to the particle-like support (e) of said co-catalyst component (d), and to use the amount of arbitration, a co-catalyst component (d) is usually the range of the 0.0001 - 1,000,000 weight section to the particle-like (support d) 100 weight section.

[0044] Next, preparation of the metallocene catalyst of this invention is explained. Preparation of the metallocene catalyst of this invention is obtained by contacting said component (A), a (metallocene compound solution), and a component (B) (support co-catalyst). A metallocene solution and a support co-catalyst may be separately introduced into the reactor which especially a limit does not have and performs a polymerization, it may be made to contact within a reactor besides contact of a component (A) and a component (B) not using aromatic hydrocarbon, and you may prepare, and after making it contact outside a reactor beforehand, it may introduce into a reactor and you may prepare.

[0045] When introducing a component (A) and a component (B) into the reactor which performs a polymerization separately and making the catalyst for polymerizations prepare within a reactor, a component (A) can be introduced into a reactor as it is, and can introduce a component (B) as a slurry of remaining as it is or aliphatic hydrocarbon. Although a co-catalyst may be added as it is in a metallocene solution when contacting a component (A) and a component (B) outside a reactor and preparing the catalyst for polymerizations, you may add as a slurry of aliphatic hydrocarbon, such as a hexane and a heptane.

[0046] Although the temperature is determined as arbitration in consideration of the conditions of the aliphatic hydrocarbon to be used or others when contacting a component (A) and a component (B) outside a reactor and preparing a polymerization catalyst, it is usually carried out in -80 degrees C - 200 degrees C. The range where contact temperature is desirable is -50 degrees C - 120 degrees C, and the still more desirable range is 0 degree C - 100 degrees C. There is especially no limit in the operating rate of a component (A) and a component (B), and when the co-catalyst component (d) in a component (B) is aluminoxane, it is usually 1-100,000 per transition-metals 1 atom in a metallocene compound (a), and by the aluminum atom. in order to acquire higher polymerization activity -- desirable -- 10-10,000 -- further -- desirable -- 50-5,000 -- it is the range of 100-1,000 most preferably.

[0047] When the co-catalyst component (d) in a component (B), an organic boron compound, the addition is usually 0.01-10,000 per transition-metals 1 atom in said metallocene compound (a). in order to acquire higher polymerization activity -- desirable -- 0.1-1,000 -- further -- desirable -- 0.3-500 -- it is the range of 0.8-100 most preferably.

[0048] The manufacture approach of the polyolefine of this invention carries out bulk polymerization of the olefin of arbitration by the liquid phase in itself to the bottom of existence of the metallocene catalyst which consists of the above-mentioned component (A) and a component (B). Although bulk polymerization here means carrying out the polymerization of the olefin in the state of the liquid phase, little content of the aliphatic hydrocarbon used in order to supply the component of the aliphatic hydrocarbon contained for a catalyst, or a catalyst and others to a polymerization reactor may be carried out at the liquid phase.

[0049] Although there is especially no limit in polymerization temperature, it is usually the range of -20 degrees C - less than 200 degrees C. It is 0-150 degrees C, the range where polymerization temperature is desirable has desirable further 20-95 degrees C, and 45 degrees C - its 85 degrees C are especially desirable.

[0050] The range of the pressure of ordinary pressure -70 kg/cm² is common, and it can choose the suitable range in consideration of the property of the polyolefine which it is going to obtain, productivity, etc. Moreover, at the time of a polymerization, molecular weight can be adjusted with the means of arbitration, such as installation of hydrogen, and selection of temperature and a pressure.

[0051]

[Effect of the Invention] According to the metallocene catalyst of this invention, the polymerization of the olefin can be carried out, without a polymerization being possible and being accompanied by fouling at the time of a polymerization, without using aromatic hydrocarbon.

[0052]

[Example] Hereafter, although an example and the example of a comparison explain this invention to a detail further, this invention is not limited to these.

[0053] The preparation co-catalyst -1 of a co-catalyst component: 70ml of toluene solutions of the methyl aluminoxane (it is 0.35 mols/l. by aluminum atom conversion) manufactured according to the well-known approach was added to the slurry which added silica (Devi Fuji Son 952 particle size: 130-micrometer, specific-surface-area:270m²/g) 3.0g to silica support ..ethyl aluminoxane toluene 50ml. After agitating at a room temperature for 1 hour, toluene was distilled off by reduced pressure. Then, it washed 5 times by the 30ml hexane, and the co-catalyst -1 was obtained.

[0054] Co-catalyst-2: Manufacture 1-BUROMO of N, silica support object 1N of N-dimethyl anilinium tris (pentafluorophenyl) (p-trichlorosilyl tetrafluoro phenyl) borate, and N-dimethyl anilinium tris (pentafluorophenyl) (p-trichlorosilyl tetrafluoro phenyl) borate - 2, 3, 5, and 6-tetrafluoro phenylbenzene 3.85g (1.86mmol) was dissolved in diethylether 50ml. Furthermore, at -78 degrees C, 10.5ml (1.6 mols/(l.)) of hexane solutions of n-butyl lithium was dropped, and it agitated for 30 minutes. The obtained solution was added in 200ml (50 mmol/liter) of hexane solutions of tris (pentafluorophenyl) borane, and the product was obtained as a solid-state by agitating for 20 minutes at 25 degrees C. The obtained solid-state was washed by the hexane after removing a solution layer, and the vacuum drying was performed. After dissolving 1.66g of solid-states obtained above in tetrahydrofuran 10ml and cooling to -78 degrees C, 1.5ml (1.6 mols/(l.)) of hexane solutions of n-butyl lithium was dropped, and it agitated for 45 minutes. It added in the solution which dissolved 2.7ml of tetrachlorosilanes in tetrahydrofuran 10ml, and this solution was agitated for 15 minutes at 25 degrees C. The tetrahydrofuran was distilled off after adding heptane 100ml to this solution. The vacuum drying of the residue which removed

the heptane layer was carried after washing by the hexane. After dichloromethane 50ml furthermore and removing insoluble matter, the 1.65g product was obtained by distilling off dichloromethane. After dissolving 1.65g of this product in dichloromethane 30ml, dimethyl anilinium chloride 0.31g was added and it agitated for 5 minutes at 25 degrees C. N and N-dimethyl anilinium tris (pentafluorophenyl) (p-trichlorosilyl tetrafluoro phenyl) borate 1.7g was obtained for dichloromethane by distilling off and carrying out a vacuum drying after removing insoluble matter.

[0055] 2) The solution made to dissolve 0.3g of compounds obtained by said 1 in dichloromethane 6ml was added to the slurry which added silica (Devi Fuji Son 952) 0.5g to support dichloromethane 30ml to silica support. After making it flow back under churning for 2 hours, the supernatant was removed, it washed by dichloromethane and the co-catalyst -2 was obtained.

[0056] Co-catalyst-3: N and N-dimethyl anilinium tris (pentafluorophenyl)

[p-(chloro dimethylsilyl) tetrafluoro phenyl] In preparation of the silica support object co-catalyst -2 of borate, after using dimethyldichlorosilane instead of tetrachlorosilane and preparing N and N-dimethyl anilinium tris (pentafluorophenyl) [p-(chloro dimethylsilyl) tetrafluoro phenyl] borate, it prepared similarly and the co-catalyst -3 was obtained.

[057] To preparation bis(cyclopentadienyl) zirconium dichloride (Tokyo formation incorporated company make) 1.0mg of an example 11 metallocene compound solution, 2ml (the Kanto chemistry incorporated company make) of commercial 1.0 mols [1.] triisobutylaluminum (it is hereafter written as TIBA.) hexane solutions and hexane 3ml were added, and the metallocene compound solution was prepared.

[0058] 2) In order to remove the impurity in 600ml an isobutane and an isobutane to the autoclave of 1.5l. of manufactures of polyethylene, in addition, the temperature up was carried out to 70 degrees C 0.5ml of 0.2 mols [1.] n-BuLi hexane solutions. What added 30mg in the above-mentioned metallocene compound solution, and agitated the aforementioned co-catalyst -1 for 3 minutes in it was pressed fit into the autoclave, subsequently ethylene was pressed fit to the pressure of 10kg/cm², the polymerization was performed for 30 minutes at the temperature of 70 degrees C, and the polyethylene particle was obtained. Fouling was not seen in the autoclave. When the gas chromatography analyzed the volatile component of the obtained polyethylene particle, aromatic hydrocarbon, such as toluene, was not detected.

[0059] To the slurry which added hexane 3ml to the preparation 1 of an example 21 ...etallocene compound solution and 2-screw (eta5-1-indenyl) ethane zirconium dichloride (product made from WITCO, Inc.) 1.0mg, 2ml (the Kanto chemistry incorporated company make) of commercial 1.0 mols [1.] TIBA hexane solutions was added, and the metallocene compound solution was prepared.

[0060] 2) It carried out like the manufacture example 1 of polyethylene, the polymerization of ethylene was performed, and the polyethylene particle was obtained. Fouling was not seen in the autoclave. When the gas chromatography analyzed the volatile component of the obtained polyethylene particle, aromatic hydrocarbon, such as toluene, was not detected.

[0061] Hexane 3ml was mixed with 2ml (the Kanto chemistry incorporated company make) of commercial 1.0 mols [1.] TIBA hexane solutions for example 31 metallocene compound solution (metallocene catalyst) preparation 1-and 2-screw (eta5-1-indenyl) ethane hafnium dichloride (product made from WITCO) 1.2mg, and the aforementioned co-catalyst -1 to 30mg, and the metallocene compound solution (metallocene catalyst) was prepared.

[0062] 2) 1.5l. of manufactures of polypropylene In order to remove the impurity in propylene 8mol and a propylene to an autoclave, in addition, the temperature up was carried out to 50 degrees C 0.5ml of 0.2 mols [1.] n-BuLi hexane solutions. The metallocene catalyst prepared by the above 1 was pressed fit into the autoclave, the polymerization was performed for 30

minutes, and the polypropylene particle was obtained. Fouling was not seen in the autoclave. When the gas chromatography analyzed the volatile component of the obtained polypropylene particle, aromatic hydrocarbon, such as toluene, was not detected.

[0063] In example 4 example 3, the screw [2-methyl-4-phenyl-(eta₅-1-indenyl)] dimethylsilane zirconium dichloride prepared according to the well-known approach instead of 1 and 2-screw (eta₅-1-indenyl) ethane hafnium dichloride was similarly carried out except having used the co-catalyst -2 instead of the co-catalyst -1. Fouling was not seen in the autoclave. When the gas chromatography analyzed the volatile component of the obtained polypropylene particle, aromatic hydrocarbon, such as toluene, was not detected.

[0064] In example 5 example 3, the 2-methyl -4 and screw [5-benzo (eta₅-1-indenyl)] dimethylsilane zirconium dichloride which were prepared according to the well-known approach instead of 1 and 2-screw (eta₅-1-indenyl) ethane hafnium dichloride were similarly carried out except having used the co-catalyst -2 instead of the co-catalyst -1. Fouling was not seen in the autoclave. When the gas chromatography analyzed the volatile component of the obtained polypropylene particle, aromatic hydrocarbon, such as toluene, was not detected.

[0065] In example 6 example 3, the 2-methyl -4 and screw [5-benzo (eta₅-1-indenyl)] dimethylsilane zirconium dichloride which were prepared according to the well-known

approach instead of 1 and 2-screw (eta₅-1-indenyl) ethane hafnium dichloride were similarly carried out except having used the co-catalyst -3 instead of the co-catalyst -1. Fouling was not seen in the autoclave. When the gas chromatography analyzed the volatile component of the obtained polypropylene particle, aromatic hydrocarbon, such as toluene, was not detected.

[0066] Although preparation of a metallocene compound solution was tried without using TIBA in example of comparison 1 example 1, the metallocene compound did not dissolve. Moreover, polyethylene was not obtained, although the liquid phase of this mixture was extracted and polyolefine was manufactured like the example 1.

[0067] In example of comparison 2 example 1, 3ml of hexane solutions of methyl aluminoxane (it is 0.35 mols/l. by aluminum atom conversion) was used instead of the co-catalyst -1, and it carried out similarly. Fouling was seen in the autoclave. When the gas chromatography analyzed the volatile component of the obtained polyethylene particle, aromatic hydrocarbon, such as toluene, was not detected.

[0068] 100mg of bis(cyclopentadienyl) zirconium dichloride was dissolved in tetrahydrofuran 5ml refined with the Na-K alloy as a preparation metallocene compound of an example of comparison 31 metallocene compound solution. After 1ml (the Kanto chemistry incorporated company make) of ether solution of one mol[l.] -methyl lithium was dropped at this solution at -20 degrees C, to the room temperature, the temperature up was carried out and it agitated for 1 hour. After adding the toluene refined with the Na-K alloy after distilling off a solvent and filtering precipitate of a lithium chloride, the obtained filtrate was distilled off and dicyclopentadienyl zirconium dimethyl was obtained. Dicyclopentadienyl zirconium dimethyl 1.2mg obtained above was dissolved in toluene 1ml, 5ml (the Kanto chemistry incorporated company make) of commercial 1.0 mols [l.] TIBA hexane solutions was added, and the solution of a metallocene compound was prepared.

[0069] 2) It carried out like the example 1 using the metallocene compound solution obtained by the manufacture above 1 of polyethylene. Fouling was seen in the autoclave. Toluene was detected when the gas chromatography analyzed the volatile component of the obtained polyethylene particle.

[0070] After dissolving preparation dicyclopentadienyl zirconium dichloride 1.2mg of an example of comparison 41 metallocene compound solution in 1ml of toluene solutions of methyl aluminoxane (it is 0.35 mols/l. by aluminum atom conversion), hexane 6ml was added and the solution of a metallocene compound was prepared.

[0071] 2) It carried out like the example 1 using the metallocene compound solution obtained by the manufacture above 1 g polypropylene. Fouling excessive in an autoclave was seen.

Moreover, the obtained polyethylene was massive. Toluene was detected when the gas chromatography analyzed a polyethylene lump's obtained volatile component.

[0072] After preparing a metallocene catalyst using toluene in the manufacture example 3 of example of comparison 51 metallocene catalyst, toluene was distilled off over 1 hour by reduced pressure. Then, hexane 5ml was added and it considered as the metallocene catalyst.

[0073] 2) Polypropylene was not obtained although the polymerization of a propylene was tried like the manufacture example 3 of polypropylene.

[0074] If an organometallic compound is not used so that the example 1 of a comparison may show, it turns out that a metallocene compound does not dissolve in aliphatic hydrocarbon, such as a hexane. Moreover, since the co-catalyst component was not supported in the example 2 of a comparison, fouling occurred. Although the example 3 of a comparison is based on the approach indicated by JP,7-2918,A, since toluene is used, toluene remains in the polypropylene with which fouling occurs and is obtained. Furthermore it is in charge of preparation of a metallocene compound solution, and the process of a large number, such as use and its purification of an ethers solvent, distilling off and a reaction with alkyl lithium, and removal of

the by-product by filtration, is needed. On the other hand, in this invention, it sees in an example -- as -- acquisition -- it is possible to attain the purpose by using the aliphatic hydrocarbon solution of a commercial metallocene compound and a commercial organometallic compound as it is in an easy metallocene compound, especially examples 1, 2, and 3. Although the example 4 of a comparison is the approach indicated by JP,8-245714,A, since toluene and the methyl aluminoxane of a solution are used, remarkable fouling occurs and it turns out that it becomes massive [the polyethylene obtained]. Moreover, toluene will remain in the obtained polyethylene. Although it was transposing to aliphatic hydrocarbon in the example 5 of a comparison after manufacturing a metallocene catalyst using aromatic hydrocarbon, the metallocene catalyst deteriorated in the process which removes aromatic hydrocarbon, and polymerization activity was hardly seen.

[Translation done.]

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3. In the drawings, any words are not translated.

DESCRIPTION OF DRAWINGS

[Brief Description of the Drawings]

[Drawing 1] It is the flow chart Fig. of metallocene catalyst preparation for polyolefine manufacture of this invention.

[Translation done.]

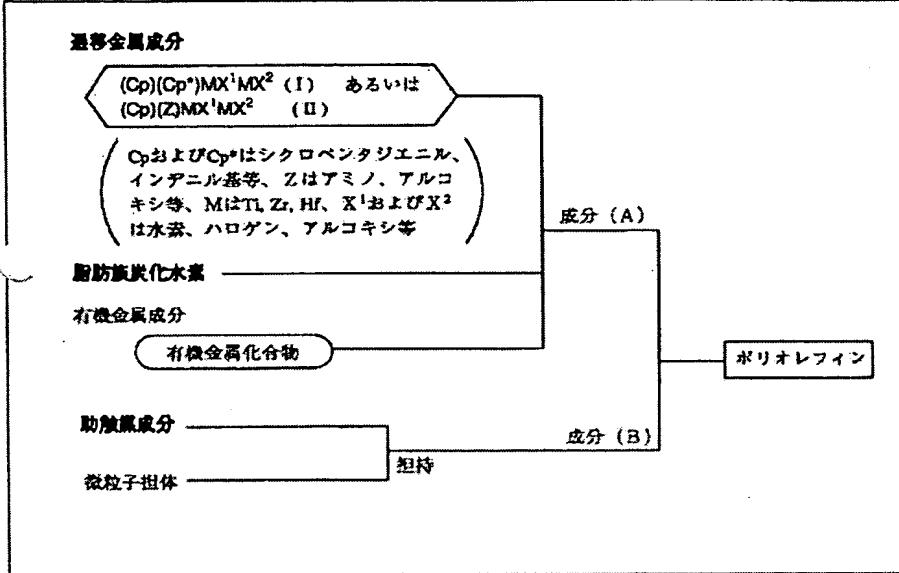
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DRAWINGS

[Drawing 1]



[Translation done.]

1/1 - (C) FILE CAPLUS

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TI - Metallocene catalysts solubilized in hydrocarbon solvents and
manufacture of polyolefins

IN - Ishigaki, Satoshi; Hikuma, Shinji; Inasawa, Shintaro; Niki, Kazumi

PA - Nippon Polyolefin K. K., Japan

SO - Jpn. Kokai Tokkyo Koho, 10 pp.

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DT - Patent

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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PN - JP10212308	A2	19980811	JP 1997-18561	19970131
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JS - MARPAT 129:217028				

AB - The catalysts are obtained by dissolving aliph. hydrocarbon-insol. metallocene compds. CpCp'MX₁X₂ or CpZMCIX₂ [Cp, Cp' = (un)substituted cyclopentadienyl or indenyl; Cp and Cp' may be linked through 1-3 at. groups selected from C, Si, Ge and Sn; Z = R₁R₂N, R₁O, R₁R₂P; R₁, R₂ = C₁-to_q.2 alkyl, alkylene, C₆-10 aryl, arylene, Si-contg. group; R₁ and R₂ may link with Cp; M = Ti, Zr, Hf; X₁, X₂ = H, halo, alkoxy, amido; _q of X₁ and X₂ is halogen] and org. metal compds. (excluding aluminoxane) in aliph. hydrocarbons, and combining with microparticle-supported cocatalysts. The polyolefins are manufd. by bulk polymn. using the catalysts in the absence of arom. hydrocarbons. Thus, polymn. of ethylene in the presence of a hexane soln. of bis(cyclopentadienyl)zirconium dichloride, (iso-Bu)₃Al and silica-supported Me aluminoxane showed no fouling on reactor walls.

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(54)【発明の名称】 ヒアルロン酸ナトリウム水溶液用安定化組成物

(57)【要約】

【構成】 ヒアルロン酸ナトリウム水溶液にヨウ素含有
の還元剤及び／又は硫黄含有の還元剤を添加されてなる
ことを特徴とするヒアルロン酸ナトリウム水溶液用安定
化組成物。

【効果】 本発明を用いることにより、ヒアルロン酸ナ
トリウム水溶液の安定化に著しい効果を奏する。

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【特許請求の範囲】

【請求項1】 ヒアルロン酸ナトリウム水溶液にヨウ素含有の還元剤及び／又は硫黄含有の還元剤を添加されることを特徴とするヒアルロン酸ナトリウム水溶液用安定化組成物。

【請求項2】 該ヨウ素含有の還元剤が金属ヨウ化化合物類であり、該硫黄含有化合物がチオ硫酸金属塩類、チオシアン酸金属塩類、チオケトン類及びスルフィド類からなる群より選ばれた化合物である請求項1記載のヒアルロン酸ナトリウム水溶液用安定化組成物。

【請求項3】 該ヨウ素含有の還元剤及び／又は硫黄含有の還元剤の添加量がヒアルロン酸ナトリウム1重量部に対し、0.001重量部以上である請求項1又は2記載のヒアルロン酸ナトリウム水溶液用安定化組成物。

【発明の詳細な説明】

【0001】

【発明の属する技術分野】 本発明はヒアルロン酸ナトリウム水溶液にヨウ素含有の還元剤及び／又は硫黄含有の還元剤を添加されてなるヒアルロン酸ナトリウム水溶液用安定化組成物に関する。

【0002】

【従来の技術】 ヒアルロン酸は、N-アセチルグルコサミン及びグルクロン酸単位の重合体であり、自然界に広く存在し、多くの哺乳類中に見出され、高保湿性、高粘弹性等の特性を有する。その特性を生かし、例えば、鶏冠から抽出させたヒアルロン酸が、変形性膝関節症の治療剤と使用され、また、ある種の微生物、例えば、ストレプトコッカス属等の微生物により発酵法で産出されたより高分子量のヒアルロン酸も、その医薬品として開発されつつある。また、ヒアルロン酸は、眼科手術時の補助剤など他の医薬用剤や化粧品としても広く使用されている。

【0003】 ところで、ヒアルロン酸は、それ自体では不安定な物質であるため、そのナトリウム塩の形で製剤化して適用されているが、ヒアルロン酸ナトリウムさえも水溶液の状態においては安定性に欠けている。ヒアルロン酸ナトリウムの水溶液は、pHによってヒアルロン酸ナトリウムの安定性が左右されると同時に、フリーラジカルや金属など存在によってもヒアルロン酸ナトリウムの分子量低下が起こり、安定性に欠ける。その安定性欠如により高粘弹性などの特性が損なわれるため、ヒアルロン酸ナトリウム水溶液の状態での保存方法が問題となっている。そこで、安定性に優れたつまりヒアルロン酸ナトリウムの分子量低下を抑制する、ヒアルロン酸ナトリウム溶液の安定化組成物が強く要望されていた。

【0004】

【発明が解決しようとする課題】 本発明者らは、このような状況のもとでヒアルロン酸ナトリウム水溶液中のヒアルロン酸ナトリウムの分子量低下を抑制し、この水溶液の安定化につき鋭意研究を進めた結果、ヒアルロン酸

ナトリウム水溶液にヨウ素含有の還元剤及び／又は硫黄含有の還元剤を添加することによってヒアルロン酸ナトリウムの分子量低下が抑制され、より安定性が増すことを見出して本発明を完成させたものである。

【0005】

【課題を解決するための手段】 すなわち、本発明は、ヒアルロン酸ナトリウム水溶液にヨウ素含有の還元剤及び／又は硫黄含有の還元剤を添加されてなることを特徴とするヒアルロン酸ナトリウム水溶液用安定化組成物である。

【0006】

本発明の好ましい実施態様としては、
(1) 該ヨウ素含有の還元剤が金属ヨウ化化合物類であり、該硫黄含有化合物がチオ硫酸金属塩類、チオシアン酸金属塩類、チオケトン類及びスルフィド類からなる群より選ばれた化合物であるヒアルロン酸ナトリウム水溶液用安定化組成物。

(2) 該ヨウ素含有の還元剤及び／又は硫黄含有の還元剤の添加量がヒアルロン酸ナトリウム1重量部に対し、0.001重量部以上であるヒアルロン酸ナトリウム水溶液用安定化組成物。が挙げられる。

【0007】

【発明の実施の形態】 以下、本発明を詳細に説明する。本発明は、ヒアルロン酸ナトリウム水溶液に対し、ヨウ素含有の還元剤及び／又は硫黄含有の還元剤をヒアルロン酸ナトリウム1重量部に対して0.001重量部以上、好ましくはヒアルロン酸ナトリウム1重量部に対して0.001～1重量部の量で配合して添加することにより、ヒアルロン酸ナトリウム水溶液の安定性を高めるものである。

【0008】 本発明に用いられるヒアルロン酸ナトリウムは、その由来は限定されるものではなく、鶏冠由来及び微生物由來のいずれも用いることができる。本発明において、ヒアルロン酸ナトリウムとしては、その分子量は特定されない。

【0009】 本発明で使用するヨウ素含有の還元剤とは、具体的にはヨウ化カリウム、ヨウ化ナトリウム、ヨウ化カルシウム、ヨウ化セシウム、ヨウ化バリウム、ヨウ化マグネシウム、及びヨウ化リチウム等の金属ヨウ化化合物類等であり、硫黄含有の還元剤とは、具体的にはチオ硫酸カリウム、及びチオ硫酸ナトリウム等のチオ硫酸金属塩類、チオシアン酸カリウム、及びチオシアン酸ナトリウム等のチオシアン酸金属塩類、チオ尿素、チオセミカルバジド、チオペントール等のチオケトン類、L-メチオニン等のスルフィド類等が挙げられる。

【0010】

【実施例】 以下実施例により本発明を更に詳しく説明する。なお、本発明はこれにより限定されるものではない。

【0011】 実施例1

ヒアルロン酸ナトリウム水溶液の調整（A液とする。）

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ヒアルロン酸ナトリウム（分子量約180万）を2mMリン酸バッファーかつ0.9%塩化ナトリウム水溶液に1重量%溶解した。

【0012】添加物溶液の調整（B液とする。）

添加物としてヨウ化カリウムを2mMリン酸バッファーかつ0.9%塩化ナトリウム水溶液に0.9重量%溶解させた。

【0013】試験方法

A液2.7mlに対し、B液を0.3ml添加した。最終的にヒアルロン酸ナトリウムの濃度0.9重量%、ヨウ化カリウムの濃度が0.09重量%になるように調整した。つまり、ヒアルロン酸ナトリウム1重量部に対し、ヨウ化カリウム0.1重量部になるように調整した。この溶液を60℃で保存し、2週間後の極限粘度を測定し、その結果からLaurentの式により平均分子量を求め、平均分子量の変化率を求めた。

【0014】実施例2

実施例1のB液における添加物としてヨウ化ナトリウムを用いた以外は実施例1と同様の試験を行った。

【0015】実施例3

実施例1のB液における添加物としてチオ硫酸ナトリウムを用いた以外は実施例1と同様の試験を行った。

【0016】実施例4

実施例1のB液における添加物としてL-メチオニンを用いた以外は実施例1と同様の試験を行った。

【0017】実施例5

実施例1のB液における添加物としてチオシアノ酸カリウムを用いた以外は、実施例1と同様の試験を行った。

【0018】実施例6

実施例1のB液における添加物としてチオ尿素を用いた以外は、実施例1と同様の試験を行った。

【0019】実施例7

添加物としてヨウ化カリウムを2mMリン酸バッファーかつ0.9%塩化ナトリウム水溶液に0.09重量%溶解させた（C液とする。）。実施例1におけるB液の替わりにC液を0.3mlをA液2.7mlに添加した。

最終的にヒアルロン酸ナトリウムの濃度0.9重量%、ヨウ化カリウムの濃度が0.009重量%になるように

調整した。つまり、ヒアルロン酸ナトリウム1重量部に対し、ヨウ化カリウム0.01重量部になるよう調整した。この溶液を実施例1と同様に60℃で保存し、2週間後の平均分子量の変化率を求めた。

【0020】実施例8

実施例7のC液における添加物としてL-メチオニンを用いた以外は実施例7と同様の試験を行った。

【0021】実施例9

添加物としてヨウ化ナトリウム、チオ硫酸ナトリウムの2種を2mMリン酸バッファーかつ0.9%塩化ナトリウム水溶液にそれぞれ0.45重量%溶解させた（D液とする。）。実施例1におけるB液の替わりにD液を添加し、実施例1と同様に60℃で保存し、2週間後の平均分子量の変化率を求めた。

【0022】実施例10

添加物としてヨウ化カリウム、L-メチオニンの2種を2mMリン酸バッファーかつ0.9%塩化ナトリウム水溶液にそれぞれ0.045重量%溶解させた（E液とする。）。実施例1におけるB液の替わりにE液0.3mlをA液2.7mlに添加した。最終的にヒアルロン酸ナトリウムの濃度0.9重量%、ヨウ化カリウム、L-メチオニンそれぞれの濃度が0.00045重量%、すなわち全添加物濃度が0.0009重量%になるよう調整した。つまり、ヒアルロン酸ナトリウム1重量部に対し、全添加物0.001重量部になるよう調整した。この溶液を実施例1と同様に60℃で保存し、2週間後の平均分子量の変化率を求めた。

【0023】比較例1

実施例の比較として添加物を添加していない実施例1のA液のみを60℃で保存し、実施例1と同時に試験を開始し、同様に2週間後の平均分子量の変化率を求めた。

【0024】比較例2～10

比較例1と同様に実施例2～10のそれぞれ比較として試験を行った。

【0025】実施例1～10及び比較例1～10の結果を表1に示す。

【0026】

【表1】

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平均分子量の変化率
(分子量約180万の検体を60°C、2週間後)

	平均分子量の変化率		平均分子量の変化率
実施例 1	81%	比較例 1	68%
実施例 2	73%	比較例 2	65%
実施例 3	76%	比較例 3	59%
実施例 4	74%	比較例 4	63%
実施例 5	79%	比較例 5	69%
実施例 6	76%	比較例 6	67%
実施例 7	73%	比較例 5	65%
実施例 8	75%	比較例 6	63%
実施例 9	83%	比較例 7	66%
実施例 10	76%	比較例 10	69%

【0027】

【発明の効果】以上のように、本発明におけるヒアルロン酸水溶液用安定化組成物は、ヒアルロン酸水溶液にヨウ素含有の還元剤及び／又は硫黄含有の還元剤が添加されることによって、著しく安定性の向上が認められた。

従って、本発明により、ヒアルロン酸ナトリウム水溶液を取り扱う際に、著しい利点をもたらし、変形性膝関節症の治療薬などの医薬品や化粧品などの長期保存安定性を増すことができる。

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